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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,527	12/30/2003	Tae-Woong Koo	070702007100	8865

7590 01/18/2007

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EXAMINER	
BERTAGNA, ANGELA MARIE	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

Interview Summary	Application No.	Applicant(s)	
	10/749,527	KOO ET AL.	
	Examiner	Art Unit	
	Angela Bertagna	1637	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Angela Bertagna*. (3)*Laura Chung*.

(2) *Ken Horlick*. (4)*Jon Baughman*.

Date of Interview: *10 January 2007*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____.

Claim(s) discussed: *1-44 and 47-49*.

Identification of prior art discussed: *Kneipp*.

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *We discussed the proposed amendments to the claims. The examiner indicated that the amendments overcome the rejections under 112, 1st paragraph made in the Final Rejection. The examiner also indicated that the claims require a new search and likely application of new/additional prior art references, because the step of separating a purine or pyrimidine base from the sugar moiety is newly presented in independent claims 24, 34 and 49*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

A. L. N. 1/10/2007
Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

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To:

NAME:	FACSIMILE:	TELEPHONE:
Angela Bertagna **Art Unit: 1637**	571-273-8291	

FROM: Laura Chung **DATE:** January 8, 2007

Number of pages with cover page:	11	

Preparer of this slip has confirmed that facsimile number given is correct: LC

Comments:

In re Patent Application of:
Tae-Woong KOO et al.
Serial No.: 10/749,527
Filed: December 30, 2003
For: NUCLEIC ACID SEQUENCING BY RAMAN...

Our Reference: 070702007100

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VA-188493

Docket No.: 070702007100
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of: Tae-Woong KOO et al.	
Application No.: 10/749,527	Confirmation No.: 8865
Filed: December 30, 2003	Art Unit: 1637
For: NUCLEIC ACID SEQUENCING BY RAMAN MONITORING OF UPTAKE OF NUCLEOTIDES DURING MOLECULAR REPLICATION	Examiner: A. M. Bertagna

DRAFT

PRELIMINARY AMENDMENT

MS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Along with the RCE application and in response to the final Action dated October 13, 2006, please amend this application as follows:

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 8 of this paper.

Va-181337

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method to detect a nucleotide or nucleoside, comprising:

separating a purine or pyrimidine base from a ribose or deoxyribose moiety of the nucleotide or nucleoside;

depositing the separated purine base or pyrimidine base on a surface enhanced Raman spectroscopy (SERS) substrate; and

~~synthesizing a double-strand molecule comprising the separated purine base or pyrimidine base and a single-strand target molecule on the SERS substrate; and~~

detecting the separated purine or pyrimidine base using SERS.

2. (Previously Presented) The method of claim 1, wherein the method detects a deoxynucleotide triphosphate.

3. (Previously Presented) The method of claim 2, wherein the method further comprises including the deoxynucleotide triphosphate in a nucleic acid sequencing reaction mixture before separating the purine or pyrimidine base from the purine or pyrimidine moiety.

4. (Previously Presented) The method of claim 1, wherein the purine or pyrimidine base is associated with a Raman label before it is detected by SERS.

5. (Previously Presented) The method of claim 1, wherein the nucleotide or nucleoside comprises a purine base.

6. (Previously Presented) The method of claim 5, wherein the base consists essentially of adenine.

7. (Previously Presented) The method of claim 5, wherein the base consists essentially of guanine.

8. (Previously Presented) The method of claim 1, wherein the surface enhanced Raman spectroscopy is surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS).

9. (Previously Presented) The method of claim 8, wherein the nucleotide or nucleoside comprises a pyrimidine base.

10. (Previously Presented) The method of claim 9, wherein the nucleotide or nucleoside comprises thymine.

11. (Previously Presented) The method of claim 9, wherein the nucleotide or nucleoside comprises uracil.

12. (Previously Presented) The method of claim 9, wherein the nucleotide or nucleoside comprises cytosine.

13. (Currently Amended) The method of claim 1, wherein the separated purine or pyrimidine base ~~single-strand target molecule~~ is deposited on silver nanoparticles.

14. (Currently Amended) The method of claim 13, wherein the separated purine or pyrimidine base ~~target molecule~~ is contacted with an alkali-metal halide salt.

15. (Previously Presented) The method of claim 14, wherein the alkali-metal halide salt is lithium chloride.

16. (Currently Amended) A method to detect a ~~single-strand~~ target molecule comprising a purine base or a pyrimidine base, comprising:

obtaining the ~~single-strand~~ target molecule;

separating a purine base or pyrimidine base from the target molecule;

depositing the separated purine base or pyrimidine base ~~target molecule~~ on a surface enhanced Raman spectroscopy (SERS) substrate;

~~synthesizing a double-strand molecule comprising a complimentary purine base or pyrimidine base and the single-strand target molecule on the SERS substrate;~~ and

detecting Raman scattering from the separated purine base or pyrimidine base ~~double-strand molecule~~ using surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS) to detect ~~a sequence of~~ the ~~single-strand~~ target molecule.

17. (Currently Amended) The method of claim 16, wherein the ~~single-strand~~ target molecule is isolated from a biological sample.

18. (Currently Amended) The method of claim 16, wherein the ~~single-strand~~ target molecule is a nucleotide[[,]] or a nucleoside~~, or a base~~.

19. (Currently Amended) The method of claim 18, wherein the ~~single-strand~~ target molecule comprises ~~consists essentially of~~ a pyrimidine base.

20. (Currently Amended) The method of claim 19, wherein the target molecule comprises ~~the base consists essentially of~~ thymine.

21. (Currently Amended) The method of claim 19, wherein the target molecule comprises ~~the base consists essentially of~~ uracil.

22. (Currently Amended) The method of claim 19, wherein the target molecule comprises ~~the base consists essentially of a~~ cytidine.

23. (Currently Amended) The method of claim 16, wherein the ~~single strand~~ target molecule is a nucleotide triphosphate.

24. (Currently Amended) A method to detect identical nucleotides at consecutive positions in a ~~complimentary to a single strand~~ template nucleic acid molecule, comprising:

contacting a known number of copies of the template ~~the single strand template~~ nucleic acid molecule with a reaction mixture comprising a primer, a polymerase, and a known initial concentration of a first nucleotide to form a post-reaction mixture, the primer or the template single strand nucleic acid being immobilized on a surface of the reaction chamber;

~~synthesizing a double strand molecule comprising the first nucleotide and the single strand template nucleic acid;~~

separating a purine or pyrimidine base from a ribose or deoxyribose moiety of the first nucleotide;

depositing the purine or pyrimidine base ~~post reaction mixture~~ on a surface enhanced Raman spectroscopy (SERS) substrate;

detecting ~~a concentration of the first nucleotide using SERS; and~~

~~determining~~ whether ~~one or~~ more than one of the first nucleotide was added to the consecutive target positions. ~~synthesized to the single strand template nucleic acid.~~

25. (Previously Presented) The method of claim 24, wherein the known number of copies of the single strand template nucleic acid molecule is about the same as a known number of first nucleotide molecules in the reaction mixture.

26. (Previously Presented) The method of claim 24, wherein the known number of copies of the single strand template nucleic acid molecule is about one half a known number of first nucleotide molecules in the reaction mixture.

27. (Currently Amended) The method of claim 24, further comprising adding additional first nucleotide to the reaction mixture after [[said]] detecting ~~the concentration of~~ the first nucleotide.

28. (Canceled).

29. (Currently Amended) The method of claim 24, wherein the ~~detecting the concentration of the first nucleotide using~~ SERS detection is surface enhanced coherent anti-Stokes Raman spectroscopy (SECARS).

30. (Previously Presented) The method of claim 24, further comprising repeating said steps of claim 24 with a different nucleotide.

31. (Previously Presented) The method of claim 24, wherein the nucleotide is attached to a Raman label before it is detected by SERS.

32. (Previously Presented) The method of claim 24, wherein an internal control is included in the reaction mixture and detected using SERS.

33. (Previously Presented) The method of claim 32, wherein the SERS signal of the internal control and the nucleotide is compared to determine whether more than one nucleotide was added to the consecutive positions complimentary to the single strand template nucleic acid molecule.

34. (Currently Amended) A method to determine a nucleotide occurrence at a target position of a ~~single strand~~ template nucleic acid molecule, comprising:

contacting a detectable number of ~~the single strand~~ template nucleic acids with a reaction mixture in a reaction chamber, the reaction mixture comprising a primer, a polymerase, and an initial concentration of a first nucleotide, the primer or the single strand template nucleic acid being immobilized on a surface of the reaction chamber;

incubating the reaction mixture to allow binding of the primer to the ~~single strand~~ template nucleic acid and formation of a post-reaction mixture;

~~synthesizing a double strand molecule comprising the first nucleotide and the single strand template nucleic acid;~~

separating a purine or pyrimidine base from a ribose or deoxyribose moiety of the first nucleotide in the post-reaction mixture;

depositing the separated purine or pyrimidine base ~~post-reaction mixture, or a component thereof,~~ on a surface enhanced Raman spectroscopy (SERS) substrate; and

detecting a Raman signal from the first nucleotide using SERS, wherein a decrease in the concentration ~~intensity of the Raman signal~~ of the first nucleotide in the post-reaction mixture identifies an extension reaction product, thereby identifying the nucleotide occurrence at the target position.

35. (Previously Presented) The method of claim 34, further comprising repeating the steps of claim 34 with a different nucleotide until the nucleotide occurrence is identified.

36. (Previously Presented) The method of claim 35, further comprising washing the SERS substrate.

37. (Previously Presented) The method of claim 34, wherein the incubation time is about 1 second to 10 minutes.

38. (Previously Presented) The method of claim 34, wherein the reaction chamber is less than 100 nm in at least one dimension.

39. (Previously Presented) The method of claim 34, wherein a pre-reaction SERS analysis is performed on the first nucleotide before it contacts the single strand template nucleic acid molecule.

40. (Canceled).

41. (Previously Presented) The method of claim 34, wherein the method is performed twice for the target position, using dATP and dGTP one at a time as the first nucleotide and a second nucleotide.

42. (Previously Presented) The method of claim 41, wherein the complementary strand of the template nucleic acid molecule is immobilized in a second reaction chamber and the method is performed an additional two times, again using dATP and dGTP one at a time as the first nucleotide and the second nucleotide.

43. (Previously Presented) The method of claim 34, wherein an internal control is included in the reaction mixture and detected using SERS.

44. (Previously Presented) The method of claim 43, wherein the SERS signal of the internal control and the nucleotide is compared to identify the nucleotide occurrence at the target position.

45. (Canceled).

46. (Canceled).

47. (Previously Presented) The method of claim 24, wherein the detecting is by monitoring a differential concentration of a purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.

48. (Previously Presented) The method of claim 34, wherein the detecting is by monitoring a differential concentration of a purine base or pyrimidine base before and after the synthesizing of the double-strand molecule.

49. (New) A method to detect a nucleotide, comprising:

obtaining a nucleic acid sequencing reaction mixture comprising a nucleotide and a partially or totally single-stranded nucleic acid molecule;

separating a purine or pyrimidine base from a ribose or deoxyribose moiety of the nucleotide;

depositing the separated purine base or pyrimidine base on a surface enhanced Raman spectroscopy (SERS) substrate; and

detecting the separated purine or pyrimidine base using SERS.

REMARKS

Applicants thank the Examiner for allowing Applicants' representatives to hold an interview on January 10, 2007.

Claims 1-15, 18-22, and 45 stand rejected under 35 USC 112 for lack of enablement. Claims 1, 13, 14, 16, 18-22 have been amended, and no longer involve the synthesis of a double-stranded nucleic acid with a separated base. Supports for these amendments are found in paragraphs 21-31 of the present application. Claim 45 has been canceled. Accordingly, Applicants respectfully request that this rejection involving claims 1-15, 18-22, and 45 be withdrawn.

Claims 1-23, 45, and 46 stand rejected under 35 USC 112 for adding new matter involving the synthesis of a double-stranded molecule with a separated base. Claims 1, 13, 14, 16, and 18-22 have been amended as mentioned above. Claims 1-23 no longer involve the synthesis of a double stranded nucleic acid with a separated base. Again, supports for these amendments can be found in paragraph 21-31 of the present application. These amendments do not add new matters. Claims 45 and 46 have been canceled. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 16, 17 and 46 stand rejected under 35 USC 103(a) on Williams in view of Vo-Dinh and further in view of Liang. Claims 16 and 17 stand rejected under 35 USC 103(a) on Xue in view of Vo-Dinh and further in view of Liang. As amended, claim 16 involves a step of separating a purine base or pyrimidine base from a target molecule, causing an enhanced Raman signal. This step is not disclosed in Williams, Vo-Dinh, Liang, or Xue.[1] Claim 46 was canceled. Accordingly, Applicants respectfully request that this rejection be withdrawn.

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[1] Please note that the office action dated April 26, 2006 stated that Kneipp teaches: (1) separating a purine or pyrimidine base from a ribose or deoxyribose moiety of a nucleotide or nucleoside (paragraph 63 of Kneipp) and (2) depositing the separated base on a SERS substrate (paragraph 63 & 48 of Kneipp). Applicants would like to point out that Kneipp actually does not disclose separating a purine or pyrimidine base from a ribose or deoxyribose moiety or depositing the separated base on a SERS substrate.

According to the specification, the separating step produces an enhanced Raman signal. Kneipp neither teaches this concept nor disclose separating a purine or pyrimidine base for SERS. Although Kneipp uses the word "base," the word is really referring to a nucleotide, not to a purine or pyrimidine base. In paragraph 63 of Kneipp,

Claims 24-28, 30-37, 39-44, 47, and 48 stand rejected under 35 USC 103(a) on Melamede in view of Kneipp and further in view of Vo-Dinh. Claim 29 stands rejected under 35 USC 103(a) on Melamede in view of Kneipp and further in view of Vo-Dinh and further in view of Liang. Claim 38 stands rejected under 35 USC 103(a) on Melamede in view of Kneipp and further in view of Vo-Dinh and further in view of Quake. Claims 24, 27, 29 and 34 have been amended, and claim 28 has been canceled. The amendments to claims 24, 27, 29, and 34 are supported by paragraphs 22, 25, 26, and 38-49 of the present application. Claims 24 and 34 as amended includes a step of separating a purine base or pyrimdine base from its sugar moiety to obtain an enhanced Raman signal. This step is not disclosed in Meladede, Kneipp, Vo-Dinh, Liang, or Quake. Accordingly, claims 24-44, 47, and 48 are in condition for allowance, and Applicants respectfully request the rejections involving these claims be withdrawn.

Claims 16-44 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting on copending Application No. 11/020,776 in view of either Willaims or Xue et al. Claims 24-44 stand provisionally rejected on the ground of nonstatory obviousness-type double patenting on copending Application No. 11/0202,776 in view of Melamede. Applicants acknowledge these rejections, but no further action is required at this time since these rejections are provisional.

Finally, claim 49 is new. Claim 49 is supported by paragraphs 21-32 of this application.

Each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a

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Kneipp recommends the use of nucleases known in the art to achieve a fragmentation of DNA or RNA molecule. Jett referred to in Kneipp also recommends the use of exonucleases to cleave individual bases from a fragment of DNA or RNA. Nucleases are phosphodiesterases. Necleases do not cleave the bond between a purine or pyrimidine base and a ribose or deoxyribose moiety. The results of using endonucleases are nucleotides or blunt or zigzag-ended fragmented DNA or RNA molecules. The results of using exonucleases are individual nucleotides, not a purine or pyrimidine base. Accordingly, the prior arguments made to overcome this rejection have been removed as it is not necessary.

telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 070702007100.

Dated: January 10, 2007

Respectfully submitted,

By_____

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